Docket No.: 80929(303655)
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Cormier et al.

Application No.: 10/045,842 Confirmation No.: 2394

Filed: October 26, 2001 Art Unit: 1762

For: TRANSDERMAL DRUG DELIVERY DEVICES HAVING COATED MICROPROTRUSIONS Examiner: E. C. Cameron

DECLARATION UNDER 37 C.F.R. §1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

I, Yuh-Fun Maa, do hereby declare as follows:

1. I am a resident of the United States. My residential address is 651 Sequoia Avenue, Millbrae, CA 94030.

2. I am currently Director, Formulation and Analytical Development, Zosano Pharma, Inc. (formerly The Macroflux Corporation), which is the licensee from Alza Corporation of the above-referenced patent application. I earned my Ph.D. in Chemical Engineering at University of Rochester (Rochester, NY). I have published >40 scholarly articles in peer-reviewed scientific journals and I am an inventor on >20 patents and patent applications in the field of pharmaceutical delivery formulations.

3. I have reviewed the Office Action dated November 27, 2007 ("the Office Action") in connection with the above-referenced patent application.

4. The cited references do not teach either expressly or implicitly the subject matter of the claimed invention in the instant application.

5. For example, the disclosure of U.S. Patent No. 5,457,041 to Ginaven et. al ("Ginaven"), does not suggest or teach the use of a coating formulation with a viscosity less than about 500 centipoise ("cp"). Ginaven does not teach how to achieve a commercially effective drying step after a micro-needle dipping process. Ginaven discloses using a highly viscous liquid such as glycerol or aqueous polyethylene glycol. The viscosity of glycerol can be as high as 934 cp at 25 deg. C, and its boiling point as high as 290 deg. C, rendering it unsuitable for evaporative

drying after being coated on the exterior surfaces of micro-needles, or after being held inside the cage-like structure at the needle tip. The formulation remains as a liquid film or drop of glycerol containing the active agent. Similarly, the aqueous polyethylene glycol in common medical use generally exists as a liquid at room temperature. A coating formulation comprised of polyethylene glycol and an active agent will therefore exist as a liquid film or drop on the surface of micro-needles.

6. Moreover, the references cited in the Office Action would not have led one of ordinary skill in the art to recognize the importance of viscosity in formulating the coating solution as claimed in the instant application. Ginaven, for example, relies primarily on capillary forces to load the coating solution onto the micro-needles. Ginaven does not specify the viscosity range or other properties necessary to improve the holding capabilities of solutions on the micro-needles. In contrast, the Macroflux® coating solution, which is based on the technology disclosed in the instant application, is designed to allow the application of a thin film of the agent-containing liquid onto the surface of the microprojections, which is then immediately dried under ambient conditions to produce a coating layer in solid form.

7. The viscosity range and the solubility parameters recited in the claims are important to the Macroflux® dip-coating process. The viscosity should be greater than 20 cp, or preferably greater than 50 cp, in order that a sufficient volume of the liquid formulation can be picked up by the microprojections during each dipping cycle. If the viscosity is too low, too much of the liquid formulation drips back into the reservoir before it can dry on the microprojections. Also, a lower viscosity level requires a greater number of dipping cycles to achieve a desired dose of the active agent in the final coating. On the other hand, if the viscosity is too high (normally greater than 200 cp, or particularly greater than 500 cp), the microprojections will pick up too much volume of the liquid formulation, leaving a large deposit of dried coating on the microprojections, compromising their ability to penetrate the skin. The large volume deposited on the microprojections with each dipping cycle also may not be sufficiently dried before the next dipping cycle, resulting in re-dissolution of the formulation into the reservoir.

8. Generally, the viscosity in the Macroflux® dip-coating process is controlled by the concentration and solubility of the drug or biological substance and excipients in the liquid formulation. A homogeneous coating solution generally depends on increasing its viscosity above 50 cp, which in turn usually requires the active agent to have a solubility greater than 50 mg/ml. A lower solubility will likely result in a viscosity less than 20 cp, which is not appropriate for the coating process claimed in the instant application.

9. I hereby further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date: 26 MAR 2008

Yuh-Fun Maa, Ph.D.